

REMARKS

Claims 1-90 are pending. Claims 1-47, 52, 53, 55, 56, 58, 60-65, 70, 71, 73, 74, 76, 77, and 81-90 are withdrawn from consideration. New claims 91 and 92 are presented herein. Support for these new claims can be found throughout the application as filed. In particular, support can be found, for example, on page 11, paragraph [037]. Claims 48-51, 54, 59-61, 66-69, 72, 75, 78-80 stand rejected.

Applicants wish to thank the Examiner for removal of the objections and rejections, in part, after consideration of Applicants' arguments in previous response. Applicants provide further remarks below and ask that the Examiner reconsider the outstanding rejections.

Rejections under 35 U.S.C. 102(b)

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75, and 78-80 under 35 U.S.C. 102(b) as being anticipated by Sem U.S. Patent 6,333,149 is respectfully traversed.

With respect to independent claim 48, the claim recites a method for obtaining a focused library of candidate binding compounds for a protein family having the following steps:

- (a) providing a ligand-probe having an antenna moiety, wherein the ligand-probe binds to the common ligand binding site of a protein, wherein the protein is a member of the protein family;
- (b) providing a sample comprising the protein, the ligand-probe and a second ligand under conditions wherein the ligand-probe, the second ligand and the protein form a bound complex;
- (c) detecting a subset of magnetization transfer signals between the antenna moiety of the ligand-probe and the second ligand in the bound complex, wherein said signals are obtained from an isotope-edited NOESY spectrum of said sample, thereby determining that the antenna moiety and second ligand are proximal in the bound complex; and
- (d) obtaining a population of candidate binding compounds comprising the ligand-probe, or a fragment thereof that binds to the common ligand binding site of said protein, covalently linked to one of a plurality of homologs of said second ligand,

whereby the population contains binding compounds that bind to members of the protein family.

Similarly, independent claim 66 recites a method for obtaining a focused library of candidate binding compounds, wherein the members of the protein family bind a common ligand, comprising the steps of:

- (a) providing a ligand-probe having an antenna moiety, wherein the ligand-probe binds to the common ligand binding site of a protein, wherein the protein is a member of the protein family;
 - (b) providing a plurality of samples comprising the protein and the ligand-probe under conditions wherein the ligand-probe and the protein form a bound complex, wherein the protein is a member of a family of proteins that bind a common ligand;
 - (c) assaying a population of candidate second ligands for the ability to transfer magnetization to the antenna moiety of the ligand-probe in a sample from the plurality, wherein said ability to transfer magnetization is assessed by determining a subset of magnetization signals of an isotope-edited NOESY spectrum of said sample;
 - (d) identifying, from the population of candidate second ligands, a second ligand that transfers magnetization to the antenna moiety of the ligand-probe, thereby determining that the two ligands are proximal to each other in a ternary bound complex with the protein; and
 - (e) obtaining a population of candidate binding compounds comprising the ligand-probe, or a fragment thereof that binds to the common ligand binding site of said protein, covalently linked to one of a plurality of homologs of said second ligand identified in step (d),
- whereby the population of candidate binding compounds contains binding compounds that bind to members of the protein family.

Applicants respectfully point out that Sem does not disclose a ligand-probe having an antenna moiety as recited in claims 48 and 66. Thus, the Examiner's statement that Sem discloses "providing a CL or common ligand attached to an isotope or antenna moiety," is not correct (Office Action at top of page 5, repeated at page 6, section 13). Furthermore, because Sem does not have an antenna moiety, step c) in claims 48 and 66 can not be performed. The

antenna moiety of claim 48 and 66 refers to a chemical group of variable length, that is attached to a ligand probe (i.e. common ligand + antenna moiety) and terminates in an isotopically labeled chemical group that permits isotope filtered NMR experiments. The antenna moiety allows one to identify a ligand (e.g. second ligand or specificity ligand) that is close (i.e. within NOE distance) to the NMR reporter atom of the antenna moiety of the ligand probe. Thus, the antenna moiety serves as an extended structure for NOE observation to an atom of a second ligand at distances further than a ligand probe (common ligand) could alone even if it were isotopically labeled. Schematically, the present application and Sem `149 compare as follows:

Ligand Probe–antenna moiety chain- $^{13}\text{CH}_3$ \leftarrow NOE OBSERVED \rightarrow atom*-Second Ligand (present application)

Ligand Probe (e.g. common ligand) \leftarrow NO NOE OBSERVED, TOO FAR \rightarrow atom*-Second Ligand (e.g. specificity ligand) (Sem `149)

Thus, with an antenna moiety the NMR reporter group is closer to the second ligand (specificity ligand) and an NOE can be observed. The absence of the antenna moiety, as in Sem `149, does not allow observation of an NOE with a second ligand, when the second ligand is beyond a certain distance.

To further clarify, Applicants point out that the linker, as described in '149, is also distinct from an antenna in that 1) the linker is not terminated in a isotope label that permits isotope filtered NMR experiments and 2) the linker is used to join common ligand and specificity ligand, to provide a bi-ligand. Regarding the first difference, Applicants note the introduction of new claims 91 and 92, which further claim specific isotopic labels that can be used in an antenna moiety.

In order for a claim to be anticipated under 35 U.S.C. 102(b) every element of the claim must be recited either explicitly or inherently. Because Sem fails to disclose providing an antenna moiety, independent claims 48 and 66 are patentable over Sem. Dependent claims 49-51, 54, 57, 59-61, 67-69, 72, 75, and 78-80 are patentable for at least the same reasons.

Double Patenting Rejections

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-33 of U.S. Patent No. 6,333,149 is respectfully traversed. Although Applicants assert the arguments provided above with respect to Sem apply to this rejection because there is no teaching or suggestion for providing a ligand probe having an antenna moiety, Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-62 of U.S. Patent No. 6,620,589 is respectfully traversed. Although Applicants assert the arguments provided above with respect to Sem apply to this rejection because there is no teaching or suggestion for providing a ligand probe having an antenna moiety, Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 1-160 of U.S. Patent No. 6,797,460 is respectfully traversed. Although Applicants assert the arguments provided above with respect to Sem apply to this rejection because there is no teaching or suggestion for providing a ligand probe having an antenna moiety, Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

The provisional rejection of claims 48-51, 54, 57, 59-61, 66-69, 72, 75 and 78-80 for obviousness-type double patenting as allegedly being unpatentable over claims 59-100 of co-pending application serial No. 10/884,181 is respectfully traversed. This patent application has now issued U.S. patent 7,252,931. Although Applicants assert the arguments provided above with respect to Sem apply to this rejection because there is no teaching or suggestion for providing a ligand probe having an antenna moiety, Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

Application No.: 10/799,934

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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